Scientific Evidence Proving Vaccines Cause Autoimmunity other than Insulin Dependent Diabetes

John Barthelow Classen, MD

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I. Introduction

It has been previously proven that vaccines cause the majority of cases of insulin dependent diabetes (IDDM), an autoimmune disease, in highly immunized populations such as children (1). The proof consists of multiple epidemiology studies and animal toxicity studies. Vaccines may cause 75% or more per cent of all cases of IDDM in children under age 10. The large magnitude by which vaccines can induce IDDM can be explained by the many different mechanisms by which vaccines can increase the risk of autoimmunity. This paper proves that common vaccines increase the risk of autoimmune diseases in general and that the effect is not limited to IDDM.

Numerous epidemiology studies have been used to provide proof that vaccines induce IDDM. Unfortunately it is impossible to perform the same quantity and quality of epidemiology studies linking vaccines to all the other autoimmune diseases. The failure to provide the same level of proof is primarily due to the lack of funds to develop precise registries of each case of each autoimmune disease in large populations. IDDM is relatively easily to study in large populations since the diagnosis is made at the time a person becomes dependent on exogenous insulin. The onset of IDDM in children is usually acute and marked by severe hyperglycemia which will be fatal in a few days if not treated . It is much harder to make a registry of all cases of other autoimmune diseases because the onset of disease is much more insidious and the diagnosis is much more arbitrary. There are literally hundreds of different autoimmune diseases. An autoimmune response is possible against almost every large molecular weight organic molecule in the body. In many if not the majority of autoimmune diseases a person can function for many decades without any treatment. In some autoimmune diseases, like allopecia and vitiligo, the disease is not fatal and the symptoms are purely cosmetic. In order to study the effect of vaccines on all autoimmune diseases beside IDDM, literally hundreds of thousands of individuals would have to be screened for hundreds of different ailments every few months for a period of 20-30 years after vaccination. This clearly is an impossible task with current resources.

Proof of an causal relationship between vaccines and autoimmune diseases, other than IDDM, can be established by proving that these autoimmune disease react in the same way as IDDM to immune stimulants including vaccines. The information below proves that common links exist between all autoimmune diseases and that autoimmune diseases react similarly to common immune stimulants. This data provides indirect proof that vaccines cause autoimmune disease.

III. Evidence of Linkage

The following text shows that the development of IDDM is closely linked with the development of other autoimmune diseases. Therefore immune stimulation that increases the risk of IDDM will increase the risk of a wide range of autoimmune diseases. The actual autoimmune disease one develops depends in part on MHC genes and other genes.

1. Antibody Studies

Patients with insulin dependent diabetes, IDDM, have an increased frequency of autoantibodies to a number of different organs. Anti-thyroid antibodies (2) (3) (4) are some of the most common organ specific autoantibodies found in diabetics. Antibodies to the stomach and adrenal glands are also common in diabetics (5) (6) (7). The reverse is also true, people with thyroid autoimmune disease have an increased frequency of anti-islet cell antibodies (8).

The linkage between IDDM and other autoimmune diseases is not limited to organ specific autoantibodies. Anti-nuclear antibodies (ANA) have been found in high frequency in patients with IDDM (9). In one study of 55 children with insulin dependent diabetes 13% were found to have ANA (10). In another study 16% of diabetics had ANA compared to 1% of controls (11). A study of patients with systemic lupus, SLE, found they had an increased risk of autoantibodies to insulin, an marker for IDDM (12).

2. Disease Linkage

Epidemiology studies show a close linkage between IDDM and other autoimmune diseases. IDDM is strongly linked with other autoimmune diseases in Type II polyglandular autoimmune syndrome (13). In this syndrome 52% of patients have diabetes mellitus , 69% have autoimmune thyroid disease and 100% have Addison's disease. Patients with IDDM and their close relatives are at increased risk for organ specific autoimmune disease (14). Some of the epidemiology data comes from studies of families where several members have autoimmune disease. Family studies indicate IDDM is linked to the development of several different autoimmune diseases including organ specific autoimmune diseases and rheumatoid diseases. Close relatives of patients with IDDM have an increased risk of a wide variety of different autoantibodies (15) (10). It has been found that depending on the family, IDDM is linked with either an increased risk of an organ specific autoimmune disease or a rheumatoid disease (16). A large study of Mennonites showed a linkage between IDDM and other autoimmune diseases including organ specific and rheumatoid diseases (17).

3. Genetics

Epidemiology has shown strong linkage of IDDM with the major histocompatability genes that control the development of immune responses. Approximately 95% of Caucasian type I diabetics express MHC class II alleles DR3 or DR4 while these alleles are expressed in only about 40% of the Caucasian population (18). The DR-3 gene is also linked to an increased risk of autoimmune thyroiditis (19). IgA deficiency, and genetic abnormality, is linked to the development of IDDM and variety of other autoimmune diseases including SLE, myasthenia gravis, rheumatoid arthritis, vitiligo, thyroiditis, Addison's disorder to mention a few (20) .

It is now believed by many that Non MHC genes have a major role in the susceptibility to developing autoimmune diseases. It has been shown that genes associated with different autoimmune diseases cluster to the same regions of the chromosome. This has led researchers to believe that clinically distinct autoimmune diseases are controlled by a common set of genes which increase the risk of IDDM other than autoimmune disorders (21) (22).

4. Viral Infections

Congenital rubella syndrome occurs when a pregnant women becomes infected with the rubella virus and the newborn develops a chronic infection with the rubella virus. Congenital rubella syndrome is strongly linked to the development of IDDM, with 40% or more of people with this syndrome developing IDDM (23-25). The syndrome is also strongly linked to the development of other autoimmune diseases (26) including thyroid disease.

5. Interferons

Immune stimulation with alpha interferon increases the risk of IDDM and a wide variety of other autoimmune diseases. People receive alpha interferon for the treatment of viral hepatitis and cancers. Alpha interferon has been repeatedly reported to cause IDDM in humans (27-30). One of 40 patients receiving alpha interferon in a Japanese study developed anti-islet cell antibodies (30). An Italian study found 14 of 11,241 patients receiving alpha interferon developed diabetes mellitus (31). Alpha interferon also increases the risk of organ specific autoimmune diseases such as thyroiditis and autoimmune rheumatic diseases such as SLE, rheumatoid arthritis, psoriasis and sarcoid (32). It has been reported that upon the administration of alpha interferon that the same patient developed both rheumatoid and organ specific autoimmune diseases (33) (34).

6. Animal Models

Animal models of human IDDM and other autoimmune diseases indicate that the other autoimmune diseases respond similarly to immune alteration as does IDDM. Vaccines have been shown to increase the risk of insulin dependent diabetes in mice (35). Vaccines have also increased the risk of other autoimmune diseases in rodents. Animal studies indicate that human vaccines can induce autoimmunity when administered with autoantigens, exacerbate autoimmunity when given alone, and can induce autoimmunity when administered without autoantigens. Freund's complete adjuvant, which contains BCG or a similar mycobacterium in mineral oil, when mixed with autoantigens is one of the strongest inducers of autoimmunity known. BCG vaccine is also been shown to exacerbate autoimmunity in lupus prone mice (36). The pertussis vaccine has been shown to be an adjuvant for a number of autoimmune diseases. The administration of the pertussis vaccine with thyroid extract in Freund's incomplete adjuvant caused the development of autoimmune thyroiditis in rats (37). The addition of pertussis vaccine also exacerbated autoimmune thyroiditis induced in rats by the administration of thyroid extract in Freund's complete adjuvant (38). Autoimmune nephritis (39) and sialadenitis (40) have been

induced in guinea pigs with pertussis vaccine and tissue homogenates. Streptococcal vaccines have been shown to induce a number of autoimmune diseases in rabbits (41-43).

The pertussis vaccine as well as other vaccines have been shown to induce demyelinating autoimmune diseases in rodents. Administration of pertussis vaccine with homogenized spinal cord caused the induction of experimental allergic encephalitis, EAE, in rats (44). Administration of the pertussis vaccine in the absence of autoantigens has been shown to exacerbate smoldering EAE in rats (45). Administration of the swine flu vaccine in combination with an neural extract has lead to the development of autoimmune neuritis (46). Live attenuated vaccines including measles, rubella, BCG and distemper vaccines have been shown to exacerbate EAE in Guinea pigs induced by the administration of homologous spinal cord in Freund's complete adjuvant (47).

Alteration of the immune system in newborn mice has a similar effect on IDDM and other autoimmune diseases. Substantial information has been accumulated in animals that transitory immune suppression or immune stimulation during the first few months of life may enhance or decrease, respectively, an animal's risk for developing insulin dependent diabetes mellitus or a classic autoimmune disease. Examples of immune stimulants which when administered in the first few weeks of life can prevent these diseases include certain infectious agents and vaccines while immune suppressants that can induce the diseases include cyclosporine. A number of papers supporting this view are discussed below as well as data suggesting these findings may have relevance to human diseases.

Studies from the 1970's showed that thymectomizing mice 2-4 days old leads to the development of autoimmune disease but thymectomy performed after 5 days failed to induce autoimmunity (48). Animals developed thyroiditis most frequently but gastritis and ovaritis were also detected in the day 2-4 thymectomized mice. Thymectomy performed during this time in different strains of mice showed that genetics influence which autoimmune disease the animals were likely to develop (49). Thymectomy in the first day of life has been shown to increase the incidence of autoimmune thyroiditis in the Buffalo strain of rats. Similar treatment at day 21 of life failed to induce an increase (50).

Administration of cyclosporine, CSA, during the first week of life induced autoimmunity in mice very similar to that occurring after day 3 thymectomy (51). Gastritis and ovaritis were detected in mice at 3 months of age as well as autoantibodies directed against these organs. Delaying the initiation of the CSA treatment until the mice were 3 days old prevented the development of autoimmunity. Adult mice given a 2 week treatment of CSA did not develop autoimmunity. These results substantiate the findings in the thymectomized mice that events occurring in the first week of life affect whether an animal develops autoimmunity later in life. The cyclosporine reference is particularly important because the immune suppression caused by CSA is transitory and reversible as opposed to the effects caused by thymectomy. Findings in the CSA study above were substantiated by a study showing that the administration of CSA to

pregnant mice caused autoimmune gastritis to develop in the offspring that had been exposed in utero (52).

It is hypothesized that thymectomy and CSA may cause autoimmunity by preventing suppresser cells from leaving the thymus and performing crucial functions needed to prevent autoimmunity. The theory is in normal animals suppresser cells leave the thymus by one week of life and perform a function that protects the animals from developing autoimmunity. Several experiments support this hypothesis. Mice thymectomized on day 3 of life were protected from developing autoimmunity if they received spleen cells from syngenic adult mice within 2 weeks of thymectomy. The administration of splenocytes at 4 weeks post thymectomy failed to prevent the development of autoimmunity (53). Similar findings were made in CSA treated mice, splenocytes from syngenic adults could prevent CSA induced autoimmunity in mice if the splenocytes were given within 2 weeks of the CSA treatment (51).

Parallel work to the above mentioned thymectomy and CSA experiments above has been performed on diabetic prone rodents. Thymectomy at day 3 of life greatly increased the incidence of diabetes in male NOD mice that usually have a low incidence of diabetes (54). Cyclosporine administration to a diabetic resistant substrain of BB rats starting at about 6 weeks of life and continuing until 22 weeks of life caused the development of diabetes in 31% of rats in the group. This finding leads the authors to believe that immune suppression has a causal relationship to diabetes in BB rats (55). Depletion of RT6.1 positive lymphocytes by administration of monoclonal antibodies starting at 30 days of life has been shown to induce diabetes in diabetes resistant strains of BB/Wor rats (56). The administration of a single transfusion splenocytes from a histocompatible diabetes resistant substrain of BB/Wor rats to diabetic prone BB/Wor was able to prevent diabetes if the transfusion was given between 27 and 46 days after birth but not if it was given at 61 days after birth (57). While diabetes prone BB/Wor rats were not thymectomized they resemble thymectomized animals because the BB/Wor rats are naturally lymphopenic.

Recent work has shown that diabetes and classical autoimmunity can be prevented in the rodent models mentioned above without transfusing immunocytes by administering lymphokines or other immune modulators before 2 months of life. A study in mice thymectomized on day 3 of life showed administration of IL-2 for 7 days, starting within 24 hours after thymectomy prevented the development of anti-gastric antibodies (54). Low doses of IL-1 and tumor necrosis factor have been shown to decrease the incidence of diabetes in BB rats (58,59) while administrations of tumor necrosis factor, IL-1 and IL-2 have all been reported to prevent diabetes in NOD mice (60-62). Administration of Freund's adjuvant, BCG vaccine, and certain lymphotrophic viruses have also been shown to prevent the development of diabetes in NOD mice.

7. Treatments

Immune suppression with different immune suppressing drugs is the standard treatment for several different autoimmune diseases. Treatment of newly diagnosed type I diabetics with cyclosporine can reverse diabetes temporarily (63,64).

8. Vaccine Induced Autoantibodies

Rises in autoantibodies have been consistently reported after vaccination. The antibodies are against a variety of different autoantigens and thus molecular mimicry does not explain the variety of autoantibodies that arise after vaccination (65-68). This indicates vaccines may alter autoimmunity by antigen nonspecific mechanisms as discussed below. Vaccines also appear to increase the frequency of anti-islet cell antibodies (69).

9. Mechanisms of Action

IDDM and other autoimmune diseases are expected to respond to immune stimulation, such as immunization, in a similar fashion because all the autoimmune diseases depend on the same cells. There is a finite number of cell types comprising the immune system and these same cell types are employed in an immune response against the pancreatic islet cells and other self tissue. Autoimmune responses employ macrophages, T lymphocytes (both helper and cytotoxic cells) and B lymphocytes. All these cells would be expected to respond similarly to immune stimulation following immunization regardless whether the immune response was directed against autoantigens on the pancreatic islet cells or other autoantigens (1).

IV. Conclusion

This document provides proof that vaccines do not just increase the risk of IDDM but increase the risk of all types of autoimmune diseases. Autoimmune diseases result from destruction of self tissue by a hyperactive immune system.

V.References

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